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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,788	03/22/2004	Steven C. Quay	03-04US	9945

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NASTECH PHARMACEUTICAL COMPANY INC
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EXAMINER

HEARD, THOMAS SWEENEY

ART UNIT	PAPER NUMBER
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1654

MAIL DATE	DELIVERY MODE
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05/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/805,788

Applicant(s)

QUAY ET AL.

Examiner

Thomas S. Heard

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) 3-7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 2 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Applicants Amendments to the claims received on 4/5/2007 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 1/8/2007 are hereby withdrawn.

Claim(s) 1-7 are pending. Applicants have amended claim(s) 1. Claims 3-7 are withdrawn. Claims 1-2 are hereby examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Claims 1 and 2 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Armour Pharmaceutical Company (EP 0115627) referred to as APC, and Moise Azria et al U.S. Patent 5,759,565, both from Applicant's IDS.

The invention is drawn to an aqueous solution of calcitonin suitable for intranasal administration consisting essentially of calcitonin, chlorobutanol at a concentration of 0.25% weight/weight, and water and having a pH of about 3.5, sodium chloride at a concentration of about 0.85% weight/weight, and optionally hydrochloric acid in an amount sufficient to adjust the pH of the solution to about 3.5, and wherein the aqueous solution has [[an]] oxygen at a content of less than about 5%.

In response to the Examiners rejection under 35 USC § 103, the Applicants have stated that the Examiner has *wrongly concluded* that Azria teach the use of chlorobutanol in a calcitonin solution. Applicants argue that Azria et al. plainly and unambiguously teaches away from using chlorobutanol in a calcitonin solution because at a concentration of 0.6% chlorobutanol "showed insufficient activity against the test fungus *Pen. Steckii*, more than 3 days being required to reduce the cell count to less than 0.1%." These statements plainly mean that chlorobutanol did not have sufficient activity as a preservative to be suitable for use in a calcitonin nasal spray and that at that concentration the Chlorobutanol attacks the rubber stopper of the spray unit. The sum of the Applicants argument on page 3 and 4 of the remarks is that Azria teaches away from the use of Chlorobutanol in a calcitonin solution.

Applicants have argued further that the Examiner has "not supplied a prima facie case for obviousness because the fact that Azria et al. teach away from use of Chlorobutanol in a calcitonin nasal spray means that "a person of ordinary skill in the art would not have been motivated to look to the EP '627 or any other reference for use of Chlorobutanol." It is also alleged that the EP '627 reference does not supply evidence

that Chlorobutanol is suitable in a calcitonin solution and that neither reference teaches degassing to achieve a oxygen concentration less than 5%.

The Applicant's arguments have been carefully considered but have not been found persuasive. Regarding the allegation that Azria teaches away from combining Chlorobutanol with calcitonin is incorrect. Azria teaches that at 0.6% has a deleterious effect but is silent at lower concentrations and EP '627 teaches these lower concentrations. Azria does not give a clear teaching that Chlorobutanol is not a desirous component to the Calcitonin solution, Azria makes a case for a single point (concentration). Regarding the Applicants assertion that "a person of ordinary skill in the art would not have been motivated to look to the EP '627 or any other reference for use of Chlorobutanol," this is also not persuasive. One who would look at the references for calcitonin solutions for nasal administration would have seen, without effort, or any preconceived notion, that Chlorobutanol has been used as a preservative. EP '627 teaches that Chlorobutanol has been used in combination with calcitonin at lower concentrations than that taught by Azria. The most likely reason that EP '627 is silent about any deleterious effects of Chlorobutanol is because EP '627 teaches the use of Chlorobutanol at lower concentrations than that of Azria. Finally, the Applicants arguments regarding degassing are not persuasive because while Azria does not teach degassing, but teaches storing the composition under an inert, nitrogenous gas, degassing is an obvious addition or substitution. Storing the solution under nitrogen, as taught by Azria at paragraph [64], clearly would denote to one of ordinary skill in the art that oxygen is an unwanted component and degassing would be a step that would be

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readily envisioned by one of ordinary skill in the art to further eliminate oxygen. In fact, bubbling the N_2 through the solution prior to storing under N_2 is also readily known to one of ordinary skill in the art. While the art is silent on the composition being at less than 5% oxygen, it is the Examiners position that oxygen would be less than 5% in the composition(s) taught by the art because oxygen is quite insoluble and envisioning even the upper end of 5% (5g of O_2 per 100 ml of water) is rather difficult. The rejection as claimed stands rejected.

As stated previously, Azria et al teaches calcitonin in a saline solution (tonicity) at a pH of 3 to 5 where the pH has been adjusted with HCl. The amount of calcitonin used in the invention is taught to be between 150 and 8,000 MRC units (I.U. of Activity) of salmon calcitonin. The composition is taught to be stored under an inert Nitrogen atmosphere for stability of the calcitonin. Chlorbutanol is also taught as being use in the nasal composition but suffers from some drawbacks when used at 0.6%. Azria et al does not teach the use of Chlorbutanol at ranges lower than that of 0.6%. See, Column 4 and lines 6-20; column 6 and lines 11-18; and column 7 and lines 32-37.

APC teaches calcitonin at a concentration range of 1 to 150 ug/ml where the concentration and dosage levels of calcitonin are with a potency of about 4000 I.U. per mg, well within the range taught by Azria et al. APC teaches the use of a Tonicity Adjuster in the range of 0.01-.5 %w/v readable upon the saline solution of Azria et al. APC also teaches the use of Chlorobutanol (a preservative) in the range of 0.001-2.0 %w/v which is instantly claimed, see page 5 and line 5-18 and page 6 for the additive ranges.

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It would have been obvious at the time of the instantly claimed invention to optimize the concentration of Chlorobutanol %w/v for any deleterious effects as the art clearly teaches the use of Chlorobutanol in combination with calcitonin. It would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum components in the claimed composition of U.S. Patent No. Armour Pharmaceutical Company (EP 0115627) and Moise Azria et al U.S. Patent 5,759,565, because the component % w/v are an art-recognized result-effective variable that is routinely determined and optimized in the composition arts. It would have been obvious to degas and store under an inert gas to increase the stability of the calcitonin in addition to the use of a Tonicity Component (saline) as taught by Azria et al. One would have been motivated to modify the composition as taught by both APC and Azria et al to optimize the concentration parameters to eliminate undesirable effect of any given component and or enhance the effect of a given component as calcitonin, saline, Chlorobutanol, as the art teaches their combination and use. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TSH



ANISH GUPTA
PRIMARY EXAMINER